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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/595,682	06/16/2000	Mary K. Danks	SJ-0005	1625

31949 7590 07/16/2002

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EXAMINER

QIAN, CELINE X

ART UNIT	PAPER NUMBER
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1636

DATE MAILED: 07/16/2002

18

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/595,682	DANKS ET AL.	
	Examiner	Art Unit	
	C. Qian	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-21 is/are pending in the application.
- 4a) Of the above claim(s) 1-11, 15-17 and 19-21 is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 12-14 and 18 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on ____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
 If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 a) ☐ All b) ☐ Some * c) ☐ None of:
 1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. ____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
 * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
 a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- | | |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s) ____. |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) ____. | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Claims 1-21 are pending in the application.

This Office Action is in response to the Amendment filed on 4/29/02.

Response to Amendment

The objection to claims 12 and 18 for depending on non-elected claims has been withdrawn in light of Applicants' amendment of the claims.

The rejection of claim 12 under 35 U.S.C. 112, second paragraph has been withdrawn in light of Applicants' amendment of the claim.

The provisional rejection of claims 12-14 and 18 under 35 U.S.C 101 for Double Patenting with claims 11-13 and 17 of application 09/622568 is held in abeyance since both applications are currently pending.

The rejection of claims 12-14 and 18 under 35 U.S.C. 112, first paragraph (enablement) is maintained for the reasons made of record in the Office Action mailed on 1/29/02 and further discussed below.

Response to Arguments

In response to the rejection of claims 12-14 and 18 under 35 U.S.C. 112, first paragraph, Applicants argue that the prior art at the time of filing teaches useful vectors, promoters, the expression level, the route of delivery, dosage amount and frequency that are effective to sensitize human tumor cell lines. Two references are introduced to demonstrate the utility of gene therapy at the time of the filing. Applicants further argue that the instant specification also teaches route of delivery of the composition recited in the claims. In addition, Applicants indicate that the dosage and schedule used in the animal experiments in example 9 and 11 would

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have been predictive for the dosage and schedule that will be used in tumor patients. Moreover, Applicants imply that the type of carboxylesterase (CE) that is claimed can be identified by computer modeling, and claim 14 limits the pro-drug to CPT and APC.

Applicant's arguments and the references introduced have been fully considered but they are not persuasive. The Examiner agrees that both prior art at the time of filing and the instant specification provide sufficient teaching of a method of sensitizing human tumor cell lines to chemotherapeutic pro-drugs by introducing a vector encoding a relevant CE to said cell lines *in vitro*, however, the non-enablement rejection is based on applying said method in an *in vivo* setting. The Examiner does not question the utility of gene therapy, as taught by the references cited by Applicants, but considers the success of gene therapy as a whole to be unpredictable for reasons discussed in the previous office action. Although the specification teaches the general delivery of the nucleic acid on page 28 as indicated by Applicants, the teaching does not overcome the unpredictability taught by the art at the time of filing (for details, please refer to the prior office action). Additionally, it is respectfully pointed out that the sensitization of tumor cells to CPT in a mouse model in example 9 relies on sufficient expression of CE in tumor cells that are transfected *in vitro*, wherein sufficient expression is ensured with subsequent antibiotic selection. This is entirely different from a patient bearing a tumor in an *in vivo* setting. It is not feasible or logical to take out the tumor from the patient and transfect the tumor with CE *in vitro*, then implant the tumor back to the patient. Further, the duration of expression of a desired protein by an adenoviral vector (as disclosed in example 11) is short. As such, it is unpredictable whether such short-term expression would be sufficient to inhibit tumor growth in a patient under chemotherapy.

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Although claim 14 has limited the chemotherapeutic pro-drug to CPT-11 and APC, the broadest claim (12) has no such limitation and encompasses all the chemotherapeutic pro-drugs that can be metabolized by a CE. In this case, rabbit liver CE and human intestinal CE metabolize CPT-11 and have the same residues that form the entrance to the active site gorge of these proteins, whether other CEs capable of metabolizing other chemotherapeutic pro-drugs would share those residues is unpredictable. Therefore, one skill in the art would have to engage in undue amount of experimentation to practice the method as claimed due to the unpredictability discussed above and in the prior office action.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Celine X Qian whose telephone number is 703-306-0283. The examiner can normally be reached on 9:00-5:30 M-F.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Remy Yucel can be reached on 703-305-1998. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-305-3014 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Celine Qian, Ph.D.

July 15, 2002



REMY YUCEL, PH.D
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600